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## **Handgrip strength is inversely associated with sudden cardiac death**

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## Research Letter

The protective role of cardiorespiratory fitness (CRF) on vascular outcomes including sudden cardiac death (SCD) is well established.<sup>1-3</sup> Emerging evidence shows that handgrip strength (HGS), a typical measure of muscular strength, is prospectively and inversely associated with mortality and vascular outcomes such as cardiovascular disease (CVD), coronary heart disease (CHD) and heart failure (HF).<sup>4,5</sup> Given the relationship between HGS and vascular outcomes, we hypothesized that HGS would be linked to the risk of SCD. HGS could be a novel risk predictor for SCD; however, the prospective association between HGS and SCD is uncertain. In a recent analysis of the Aerobics Center Longitudinal Study, Jiménez-Pavón and colleagues demonstrated moderate muscular strength to be protective against SCD risk;<sup>6</sup> however this study was limited by the low event rate (23 SCD cases). In this context, we aimed to assess the association between HGS and risk of SCD in a population-based prospective cohort of 861 men and women with a relatively higher event rate.

The Kuopio Ischemic Heart Disease (KIHD) risk factor study was set up to investigate potential risk factors for CVD outcomes.<sup>7</sup> Study recruitment, baseline examinations (March 1998 to December 2001) and the diagnostic classification of SCDs have been described previously.<sup>8</sup> HGS was measured by a hand dynamometer (in kPa; Martin-Balloon-Vigorimeter; Gebrüder Martin, Tuttlingen, Germany). Two measurements were taken for the dominant hand and the mean of both values was used for analysis. Values of HGS were divided by weight in kilograms to yield relative HGS (kPa/kg). The study protocol was approved by Research Ethics Committee of the University of Eastern Finland, Kuopio, Finland, in line with the Helsinki Declaration and every participant provided written informed consent. We included all SCDs that occurred from study enrollment through to 2017. Hazard ratios (HRs) with their 95%

confidence intervals (CIs) for SCD were calculated using Cox proportional hazard models. All statistical analyses were conducted using Stata version MP 16 (Stata Corp, College Station, Texas, USA).

The mean (standard deviation, SD) age of study participants at baseline was 69 (3) years and 47.3% comprised of males. The mean (SD) value of relative HGS at baseline was 1.03 (0.34) kpa/kg. During a median (IQR) follow-up of 17.3 (12.6-18.4) years, 50 SCDs occurred. Cumulative hazard curves demonstrated a lower risk of SCDs among participants in the upper median of HGS levels compared to those in the lower median ( $P=.001$  for log-rank test; **Figure 1a**). The age- and sex-adjusted HR per 1 SD increase in relative HGS was 0.52 (95% CI: 0.34-0.79), which persisted on additional adjustment for systolic blood pressure, total and high-density lipoprotein cholesterol and history of type 2 diabetes 0.52 (95% CI: 0.33-0.81). Comparing the top versus bottom medians of relative HGS levels, the corresponding adjusted HRs were 0.47 (95% CI: 0.25-0.59) and 0.51 (95% CI: 0.28-0.95), respectively (**Figure 1b**).

In this first prospective study of the association between relative HGS and risk of SCD, relative HGS was inversely and independently associated with future risk of SCDs. It has been speculated that the protective effect of higher muscle strength (assessed by HGS) on CVD mortality may be mediated by reduction in incidence of weight gain, abdominal adiposity, insulin resistance, and inflammation.<sup>9</sup> Hence, given the close inter-relationship between muscle strength, CHD and SCD, we postulate that similar pathways may underlie the relationship between HGS and risk of SCD. The current findings are relevant and adds to the existing evidence that HGS, a measure of body muscle strength, promotes vascular benefits. The assessment of HGS is simple and not time-consuming compared to other physical fitness assessments.

Strengths of the current evaluation include its novelty, long-term and complete follow-up of participants, and the representative sample of middle-aged to elderly men and women. Some study limitations include the low event rate for SCDs which precluded analyses such as the dose-response

relationship and effect modification and the inability to adjust for relevant confounders such as socioeconomic status and CRF. However, we took into account the levels of resting heart rate and physical activity in our multivariable analyses. In conclusion, this study suggests that relative HGS is inversely associated with future risk of SCDs. Further research is needed to evaluate whether assessment of HGS levels can be used to identify individuals at high risk of SCD.

**Disclosures:** All authors have no conflicts of interest to disclose.

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## References

1. Jimenez-Pavon D, Lavie CJ, Blair SN. The role of cardiorespiratory fitness on the risk of sudden cardiac death at the population level: A systematic review and meta-analysis of the available evidence. *Prog Cardiovasc Dis*. 2019;62:279-287.
2. Laukkanen JA, Lavie CJ, Khan H, Kurl S, Kunutsor SK. Cardiorespiratory Fitness and the Risk of Serious Ventricular Arrhythmias: A Prospective Cohort Study. *Mayo Clin Proc*. 2019;94:833-841.
3. Laukkanen J, Laukkanen T, Khan H, Babar M, Kunutsor SK. Combined effect of sauna bathing and cardiorespiratory fitness on the risk of sudden cardiac deaths in Caucasian men: a long-term prospective cohort study. *Prog Cardiovasc Dis*. 2018 Mar 15. pii: S0033-0620(18)30058-6.
4. Celis-Morales CA, Lyall DM, Anderson J, et al. The association between physical activity and risk of mortality is modulated by grip strength and cardiorespiratory fitness: evidence from 498 135 UK-Biobank participants. *Eur Heart J*. 2017;38:116-122.
5. Cooper R, Kuh D, Hardy R, Mortality Review G, Falcon, Teams HAS. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ*. 2010;341:c4467.
6. Jiménez-Pavón D, Brellenthin AG, Lee DC, Blair SN, Lavie CJ. Role of Muscular Strength on the Risk of Sudden Cardiac Death in Men. *Mayo Clinic proceedings*. 2019 94:2588-2590.
7. Laukkanen JA, Makikallio TH, Rauramaa R, Kiviniemi V, Ronkainen K, Kurl S. Cardiorespiratory fitness is related to the risk of sudden cardiac death: a population-based follow-up study. *J Am Coll Cardiol*. 2010;56:1476-1483.
8. Kunutsor SK, Blom AW, Whitehouse MR, Kehoe PG, Laukkanen JA. Renin-angiotensin system inhibitors and risk of fractures: a prospective cohort study and meta-analysis of published observational cohort studies. *Eur J Epidemiol*. 2017;32:947-959.
9. Artero EG, Lee DC, Lavie CJ, et al. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev*. 2012;32:351-358.

**Commented [LJ1]:** 5 new references (10 is maximum):

Role of Muscular Strength on the Risk of Sudden Cardiac Death in Men David Jiménez-Pavón, Angelique G. Brellenthin, Duck-chul Lee, Xuemi Sui, Steven N. Blair, Carl J. Lavie. *Mayo Clin Proc*. December 2019 Volume 94, Issue 12, Pages 2589–2591

Association of Fitness and Grip Strength With Heart Failure: Findings From the UK Biobank Population-Based Study Anne Sillars, Carlos A. Celis-Morales, Frederick K. Ho, Fanny Petermann, Paul Welsh, Stamatina Iliodromiti, Lyn D. Ferguson, Donald M. Lyall, Jana Anderson, Daniel F. Mackay, Pierpaolo Pellicori, John Cleland, Jill P. Pell, Jason M.R. Gill, Stuart R. Gray, Naveed Sattar. *Mayo Clin Proc*. November 2019 Volume 94, Issue 11, Pages 2230–2240

Cardiorespiratory Fitness and the Risk of Serious Ventricular Arrhythmias: A Prospective Cohort Study. Laukkanen JA, Lavie CJ, Khan H, Kurl S, Kunutsor SK. *Mayo Clin Proc*. 2019 May;94(5):833-841.

Not sure if we could put our just accepted CRF and mortality from UK Biobank (as In press 2020)

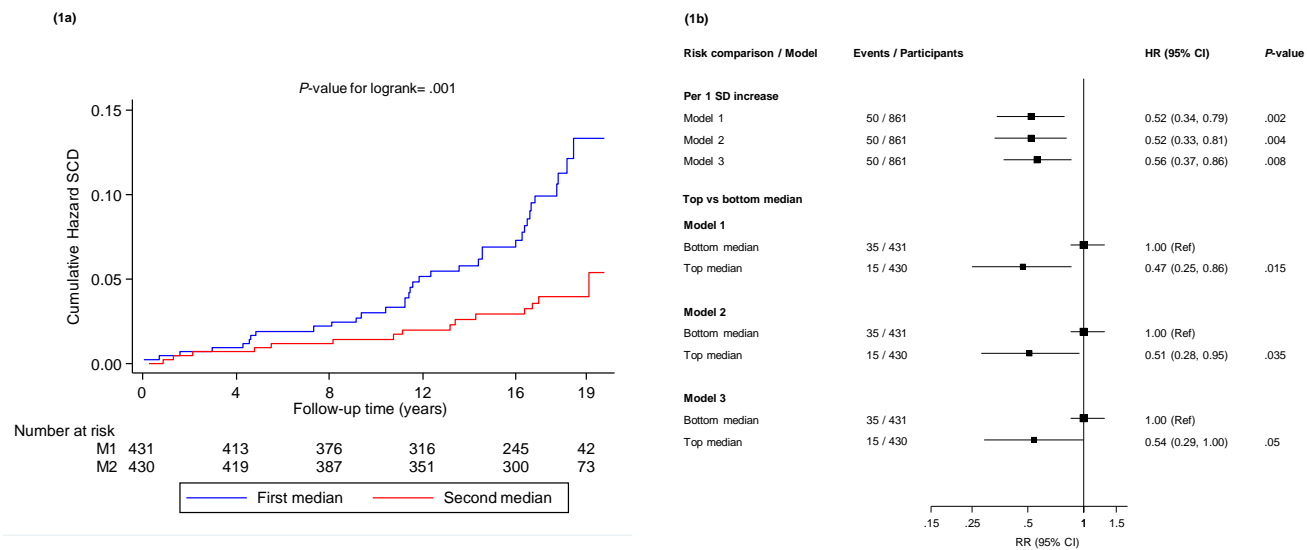
Other possible on SCD/HG and outcomes

Combined Effect of Sauna Bathing and Cardiorespiratory Fitness on the Risk of Sudden Cardiac Deaths in Caucasian Men: A Long-term Prospective Cohort Study. Laukkanen JA, Laukkanen T, Khan H, Babar M, Kunutsor SK. *Prog Cardiovasc Dis*. 2018 Mar - Apr;60(6):635-641

Celis-Morales CA, Lyall DM, Anderson J et al. The association between physical activity and risk of mortality is modulated by grip strength and cardiorespiratory fitness: evidence from 498 135 UK-Biobank participants. *Eur Heart J* 2017;38:116-122.

Figure Legends

Figure. Associations of relative handgrip strength with sudden cardiac death



(1a), Cumulative hazard curves for sudden cardiac death by medians of relative handgrip strength; (1b), Hazard ratios of relative handgrip strength for sudden cardiac death  
CI, confidence interval; HR, hazard ratio; SD, standard deviation  
Model 1: Adjusted for age and gender  
Model 2: Model 1 plus systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, and history of type 2 diabetes  
Model 3: Model 1 plus resting heart rate, smoking status, prevalent coronary heart disease, and physical activity